Supporting Information of

Excess Relative Risk as an Effect Measure in Case-Control Studies of Rare Diseases

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S3 Exhibit. Estimation of population attributable fraction (PAF) and attributable fraction among the exposed population (AFE) under heterogeneity.

Under heterogeneity,

$$\widehat{\mathrm{AFE}}_{\mathrm{het}} = \frac{\widehat{\mathrm{Risk}}_{E=1} - \sum_{s=1}^{L} \widehat{\Pr}\left(S=s \mid E=1\right) \times \widehat{\mathrm{Risk}}_{s,2}}{\widehat{\mathrm{Risk}}_{E=1}}$$

$$= \frac{f \times \dfrac{\mathrm{CS}_{+,1}}{\mathrm{CN}_{+,1}} - \sum_{s=1}^{L} \dfrac{\mathrm{CN}_{s,1}}{\mathrm{CN}_{+,1}} \times f \times \dfrac{\mathrm{CS}_{s,2}}{\mathrm{CN}_{s,2}}}{f \times \dfrac{\mathrm{CS}_{+,1}}{\mathrm{CN}_{+,1}}}$$

$$= \left(\mathrm{CS}_{+,1} - \sum_{s=1}^{L} \frac{\mathrm{CS}_{s,2} \times \mathrm{CN}_{s,1}}{\mathrm{CN}_{s,2}} \right) \Big/ \mathrm{CS}_{+,1}$$

$$= \sum_{s=1}^{L} \frac{\mathrm{CN}_{s,1}}{\mathrm{CN}_{+,1}} \times \left(\frac{\mathrm{CS}_{s,1}}{\mathrm{CN}_{s,1}} - \frac{\mathrm{CS}_{s,2}}{\mathrm{CN}_{s,2}} \right) \times \frac{\mathrm{CN}_{+,1}}{\mathrm{CS}_{+,1}}$$

$$= \sum_{s=1}^{L} \frac{\mathrm{CN}_{s,1}}{\mathrm{CN}_{+,1}} \times \hat{\phi}_s .$$

Using Miettinen's case-based formula (see Miettinen OS. Proportion of disease caused or prevented by a given exposure, trait or intervention. Am J Epidemiol. 1974;99:325–332),

$$\widehat{\mathrm{PAF}}_{\mathrm{het}} = (\text{exposure prevalence among cases}) \times \widehat{\mathrm{AFE}}_{\mathrm{het}}$$

$$= \frac{\mathrm{CS}_{+,1}}{n_1} \times \sum_{s=1}^{L} \frac{\mathrm{CN}_{s,1}}{\mathrm{CN}_{+,1}} \times \left(\frac{\mathrm{CS}_{s,1}}{\mathrm{CN}_{s,1}} - \frac{\mathrm{CS}_{s,2}}{\mathrm{CN}_{s,2}} \right) \times \frac{\mathrm{CN}_{+,1}}{\mathrm{CS}_{+,1}}$$

$$= \sum_{s=1}^{L} \frac{\mathrm{CN}_{s,1}}{\mathrm{CN}_{+,1}} \times \left(\frac{\mathrm{CS}_{s,1}}{\mathrm{CN}_{s,1}} - \frac{\mathrm{CS}_{s,2}}{\mathrm{CN}_{s,2}} \right) \times \frac{\mathrm{CN}_{+,1}}{n_1}$$

$$= \sum_{s=1}^{L} \frac{\mathrm{CN}_{s,1}}{\mathrm{CN}_{+,1}} \times \hat{\psi}_s .$$